REMARKS

Claims 1-34 are pending. By this Amendment, claims 1 and 22 are amended. No new matter is added.

This Amendment includes marked-up copies of each rewritten claim (37 C.F.R. §1.121(c)(1)(ii)).

I. Claim Amendments

Claims 1 and 22 are amended to recite "closing the container after step a) and maintaining the container closed until the obtainment of the desired amount of amplified product," and "wherein after step a), all steps are performed in the closed container, without subsequent addition of any ingredients." Support can be found in the original patent (i.e., U.S. Patent No. 5,817,465) at least at columns 1 and 3.

II. Sequence Listing

The Office Action objects to the specification for failing to meet the Patent Office's sequence listing rules. In accordance with 37 C.F.R. §1.821(e), Applicants request that the Patent Office use the computer-readable sequence listing from the original application, which issued as U.S. Patent No. 5,817,465 on October 6, 1998.

The computer-readable form in this application, 09/680,946, is identical with that filed in Application No. 08/412,229, filed September 12, 1997. In accordance with 37 C.F.R. §1.821(e), please use the only computer readable form filed in that application as the computer readable form for the instant application. It is understood that the U.S. Patent and Trademark Office will make the necessary changes in application number and filing date for the computer readable form that will be used for the instant application. A paper copy of that sequence listing is attached to this Amendment for entry into the originally filed specification of the instant application.

Thus, the requirements of 37 C.F.R. §1.821(c) have been met. Reconsideration and withdrawal of the objection are respectfully requested.

III. Double Patenting

Claims 1-34 are rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,654,143. The attached Terminal Disclaimer is concurrently filed in compliance with 37 C.F.R. §1.321(c) in order to overcome this rejection. Reconsideration and withdrawal of the rejection are respectfully requested.

IV. Reissue Rejections

Claims 1-34 are rejected under 35 U.S.C. §251 as being broadened in a reissue application filed more than two years from the issue date of the original patent. Applicants respectfully traverse the rejection.

The Office Action specifically states that the "claims are being broadened in an application filed more than two years after the issue of U.S. Patent 5,654,143." 35 U.S.C. §251 requires that no reissued patent shall be granted enlarging the scope of the claims of the original patent unless applied for within two years from the grant of the original patent. The original patent for the instant reissue application is U.S. Patent No. 5,817,465, which issued October 6, 1998. Thus, the determination of whether the reissue application was filed within two years from the grant of the original patent should be made with respect to the issue date of U.S. Patent No. 5,817,465, and **not** the issue date of U.S. Patent No. 5,654,143. The instant reissue application was filed October 6, 2000, i.e., within two years from the grant of the original Patent No. 5,817,465. Thus, the reissue rejection is improper as a matter of law. Reconsideration and withdrawal of the reissue rejection are respectfully requested.

V. §102 Rejections

A. Rejections Over Sellner

Claims 1, 3, 4, 8-12, 14, 19, 22-25 and 27-34 are rejected under 35 U.S.C. §102(b) as being anticipated by Sellner et al. (Sellner). Applicants respectfully traverse the rejection.

Claims 1 and 22 are listed above in the Amendments to the Claims section.

Sellner does not teach a method that includes heating a starting solution to a temperature not to exceed 75°C for a sufficient time to provide denaturation of said RNA without activating the enzyme system having reverse transcriptase activity, as required by step (b) of claim 1. In addition, Sellner does not teach a method that includes heating a starting solution to a temperature sufficient to permit denaturation of secondary structures that may be present in RNA but not above 75°C for a time sufficient to permit denaturation of secondary structures without completely inactivating the reverse transcriptase activity, as required by step (b) of claim 22.

In contrast to the claimed invention, Sellner discloses a system in which all the reagents required for both reverse transcription and amplification can be added to one tube and a single "non-interrupted" thermal cycling program can be performed. See page 1488, left column, of Sellner. Sellner discloses (1) submitting a solution containing the viral RNA, primers, dNTPs, TAQ polymerase and AMV-RT to a temperature of 42° C for 60 minutes to allow reverse transcription, (2) submitting the solution to a temperature of 94° C for 5 minutes to denature the DNA, (3) submitting the solution to 35 cycles of 94° C for one minute, 60° C for one minute for primer annealing and 72° C for primer extension, and (4) submitting the solution to 72° C for seven minutes. Sellner does not teach a step of denaturing the RNA without inactivating the enzyme system having reversed transcriptase activity (step (b) of claims 1 and 2) before reverse transcription (step (c) of claims 1 and 2). See page 1488, left column, of Sellner.

In fact, Sellner teaches away from the claimed invention by requiring a non-interrupted protocol that begins with reverse transcription, followed by denaturation of the DNA generated by the reverse transcription, 35 cycles of DNA amplification, and a final incubation period. Sellner's non-interrupted protocol does not include a heating step for denaturing the RNA without inactivating the enzyme system having reverse transcriptase activity, before the reverse transcription step, as required by claims 1 and 22.

For at least the reasons discussed above, Sellner does not teach or suggest every feature of claims 1 and 22. Thus, Sellner does not anticipate claims 1 and 22. Claims 3, 4, 8-12, 14, 19, 23-25 and 27-34 depend from claim 1 or claim 22, and thus include all of the features of claim 1 or claim 22. Accordingly, these dependent claims are not anticipated by Sellner for at least the same reasons as claims 1 and 22, as well as for their own features. Reconsideration and withdrawal of the rejection are respectfully requested.

In particular, dependent claim 9 recites that the ratio of units of reverse transcriptase to units of DNA polymerase is from 2 to 8, and claim 10 recites that this ratio is from 2 to 6. Sellner does not teach either of these claimed ratios.

The Office Action cites Sellner's disclosure at page 1488, col. 2, as teaching a ratio of units of reverse transcriptase to units of DNA polymerase of from 2 to 4. However, the Office Action has incorrectly interpreted Sellner's disclosure, for at least the reasons discussed below.

Sellner discloses RT-PCR performed with 2 units of Taq polymerase and 5, 4, 3, 2, 1, 0.5 or 0 units of reverse transcriptase. Sellner discloses further that reactions with 3 units or less of reverse transcriptase were successful. Accordingly, Sellner only discloses that reactions using a ratio of reverse transcriptase to Taq polymerase equal to or less than 3:2 **(i.e., a ratio of 1.5)** are successful.

In addition, Sellner discloses reactions using 7 units of reverse transcriptase and 2, 5, 10 or 15 units of Taq polymerase. Sellner only discloses that reactions containing 5 units of Taq polymerase or greater were successful. Accordingly, Sellner discloses that the only successful reactions use a ratio of reverse transcriptase to Taq polymerase of less than or equal to 7:5 **(i.e., a ratio of 1.4)**. Sellner confirms these conclusions by disclosing at the end of that paragraph that "these reactions show that reverse transcriptase is able to block Taq polymerase activity if the reverse transcriptase to Taq polymerase ratio is greater than approximately 3:2." Accordingly, Sellner only discloses using a reverse transcriptase to Taq

polymerase ratio equal to or less than 1.5, and Sellner does not teach a ratio of from 2 to 8 or 2 to 6 as required by claims 9 and 10, respectively.

For at least these reasons, Sellner does not teach every feature of claims 9 and 10. Accordingly, claims 9 and 10 are not anticipated by Sellner.

B. Rejections Over Myers

Claims 1-4, 7, 11, 12, 14, 18-23 and 26-34 are rejected under 35 U.S.C. §102(b) as being anticipated by Myers et al. (Myers). Applicants respectfully traverse the rejection.

Claims 1 and 22 are discussed above.

Myers does not teach (a) obtaining a starting solution by adding to/placing in a container comprising the sample: a buffer, a first primer, a second primer, a plurality of nucleotide triphosphates, and a sufficient amount of an enzyme system having reverse transcriptase activity and a heat stable enzyme system having DNA polymerase activity or an enzyme system having reverse transcriptase activity and DNA polymerase activity,

and closing the container after step a) and maintaining the container closed until the obtainment of the desired amount of amplified product, wherein after step a), all steps are performed in the closed container, without subsequent addition of any ingredients, as required by claims 1 and 22.

At page 7662, right column, in the paragraph entitled "RT/PCR Coupled Reactions," Myers discloses carrying out the RT reaction with *Tth* polymerase in the presence of $MnCl_2$, and discloses adding a solution containing $MgCl_2$ and EDTA following the reverse transcription reaction. Thus, Myers teaches away from the claimed invention by requiring the subsequent addition of ingredients after reverse transcription.

For at least these reasons, Myers does not teach every feature of claims 1 and 22. Accordingly, Myers does not anticipate claims 1 and 22. Claims 2-4, 7, 11, 12, 14, 18-21, 23 and 26-34 depend from claim 1 or claim 22, and thus include all of the features of claim 1 or claim 22. Accordingly, the dependent claims are not anticipated by Myers for at least the

same reasons as claims 1 and 22. Reconsideration and withdrawal of the rejection are respectfully requested.

VI. §103 Rejections

Claims 2, 5-7, 13, 18, 20, 21 and 26 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sellner in view of Shimomaye et al. (Shimomaye). Applicants respectfully traverse the rejection.

Claims 1 and 22, and Sellner are discussed above. Shimomaye does not overcome the deficiencies of Sellner.

Specifically, Shimomaye does not teach a method that includes heating a starting solution to a temperature not to exceed 75°C for a sufficient time to provide denaturation of said RNA without activating the enzyme system having reverse transcriptase activity, as required by step (b) of claim 1. In addition, Shimomaye does not teach a method that includes heating a starting solution to a temperature sufficient to permit denaturation of secondary structures that may be present in RNA but not above 75°C for a time sufficient to permit denaturation of secondary structures without completely inactivating the reverse transcriptase activity, as required by step (b) of claim 22.

At page 27, in the experimental section at the paragraph entitled "AMVRT Reaction Conditions," Shimomaye discloses that the RNA template was denatured with the radioactive oligonucleotides at 100° C for 3 minutes and allowed to anneal for 30 minutes at 42° C. Shimomaye discloses that it is only to the annealed mix that the AMVRT is added. Thus, Shimomaye requires that the RNA is first denatured by heat treatment in the absence of the reverse transcriptase and does not teach or suggest the denaturing the RNA template in the presence of AMVRT without completely inactivating the reverse transcriptase activity, as required by claims 1 and 22 of the instant application.

For at least these reasons, Sellner, alone or in combination with Shimomaye, does not teach or suggest every feature of claims 1 and 22. Thus, claims 1 and 22 are patentable over

Sellner, alone or in view of Shimomaye. Claims 2, 5-7, 13, 18, 20, 21 and 26 depend from claim 1 or claim 22, and thus include all of the features of claim 1 or claim 22. Accordingly, the dependent claims are patentable over Sellner, alone or in view of Shimomaye, for at least the same reasons as claims 1 and 22. Reconsideration and withdrawal of the rejection are respectfully requested.

VII. Conclusion

In view of the foregoing amendments and remarks, Applicants submit that this application is in condition for allowance. Favorable reconsideration and prompt allowance of claims 1-34 are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number set forth below.

Respectfully submitted,

William P. Berridge
Registration No. 30,024

Philip A. Caramanica, Jr.
Registration No. 51,528

WPB:PAC/amw

Attachments:
Sequence Listing (paper copy)
Terminal Disclaimer

Date: May 13, 2003

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461